



## ABSTRACT

**BACKGROUND:** Acne is a multifactorial disorder, and stress potentially plays a role in its pathogenesis. **OBJECTIVES:** We aimed to assess the serum levels of neurotensin in patients with acne vulgaris (AV) and investigate the relationship of these levels to quality of life (QoL), depression, anxiety, and stress. **METHODS:** The study included 60 patients with AV classified into mild (n=20), moderate (n=20), and severe (n=20) groups and 20 healthy, age-matched, sex-matched, and body mass index (BMI)-matched individuals in a control group. Patient QoL was assessed using the Dermatology Life Quality Index (DLQI). Each participant completed the Hospital Anxiety and Depression Scale (HADS) and Perceived Stress Scale (PSS-10). Serum levels of neurotensin were measured with enzyme-linked immunosorbent assay (ELISA). **RESULTS.** Neurotensin levels and scores from the three questionnaires were significantly higher among the patients with AV than the control subjects. They were also significantly elevated in patients with post-acne scars and hyperpigmentation and in those with severe acne. **CONCLUSION:** It is well known that acne greatly impacts QoL and might be associated with depression, anxiety, and stress. Further, serum neurotensin could be a promising marker to objectively evaluate the psychosocial impact of AV.

**KEYWORDS:** Acne, anxiety, depression, neurotensin, quality of life

# Serum Neurotensin: An Objective Mirror to Acne-induced Quality of Life and Psychological Impairment

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Acne vulgaris (AV) is a widespread multifactorial disorder of pilosebaceous elements, and its pathogenic factors (i.e., follicular hyperkeratosis, increased activity of sebaceous glands, microbe hypercolonization, inflammation, and immune response) are commonly known. Psychological factors have become a subject of special concern, and stressful situations are discussed as possible triggering factors of acne.<sup>1</sup> Adolescent patients with acne have reported low self-esteem and symptoms of depression, leading to a lower quality of life (QoL). Psychological comorbidities, including depression and anxiety, have largely been associated with AV, but it is unclear whether AV is the cause, or if it only worsens the preexisting conditions.<sup>2</sup>

Neuropeptides are present in the skin, where they might play a role as neurotransmitters and trophins.<sup>3</sup> In the present work, we aimed to assess the serum levels of neurotensin in patients with AV and investigate their relationship to QoL, depression, anxiety, and stress as evaluated by the Dermatology Life Quality Index (DLQI), Hospital Anxiety and Depression Scale (HADS), and Perceived Stress Scale (PSS-10), respectively.

## METHODS

**Subjects.** This case control study was approved by the local ethics committee on research involving human subjects of Benha Faculty of Medicine. Informed consent was obtained from all participants before sample collection.

The study included 60 patients with AV classified into three groups (mild, moderate, and severe acne) with 20 patients in each group. In addition, 20 apparently healthy, age-, sex-, and body mass index (BMI)-matched subjects were included as a control group. Subjects were recruited from the dermatology outpatient clinic in Benha University Hospital. Pregnant and lactating women and patients suffering from any chronic skin or systemic diseases, concurrent psychiatric illness, or receiving any regular psychotropic medication or antidepressant drugs were excluded from this work.

All patients were subjected to a detailed history taking and physical examination to evaluate the clinical type and severity of acne using the Global Acne Grading System (GAGS).<sup>4</sup> The patients' QoL was assessed using the DLQI, a validated questionnaire containing 10 questions evaluating symptoms, feelings, and the impact of the skin condition on daily activities, leisure, work and school, personal relationships, and

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treatment.<sup>5</sup>

Each participant completed the HADS, which assesses depression and anxiety,<sup>6</sup> and the PSS-10, which assesses the stress experienced by the patients.<sup>7</sup> Serum levels of neurotensin were measured for all enrolled subjects using the Human Neurotensin (NT) ELISA Kit (INOVA; Beijing, China) Cat No. CSBE09144h, according to the manufacturer's instructions.

**Statistical analysis.** The collected data were summarized in terms of mean  $\pm$  standard deviation (SD), median and range for quantitative data as appropriate, and frequency and percentage for qualitative data. Comparisons between the different study groups were carried out using the Fisher's Exact Test (FET) to compare differences between proportions, and the Student's *t*-test (*t*) and the Mann-Whitney test (*Z*) were used to test differences between two groups regarding parametric and nonparametric data, respectively. The one-way analysis of variance (ANOVA;*F*) and the Kruskal-Wallis test (*X*<sup>2</sup>) were used to compare more than two groups as appropriate, followed by *post-hoc* testing using the Bonferroni method to detect differences in pairs. Spearman correlation coefficient ( $\rho$ ) was used to assess correlations between quantitative variables as appropriate.

Statistical significance (*S*) was accepted at *P*-value  $< 0.05$ . A *P*-value  $< 0.001$  was considered highly significant (HS) while a *P*-value  $> 0.05$  was considered nonsignificant. All statistical analyses were carried out in STATA/SE version 11.2 for Windows (STATA Corporation, College Station, Texas).

## RESULTS

The study was conducted on 60 patients with AV, 50 female participants (83.3%) and 10 male participants (16.6%). Their mean age was  $20.9 \pm 2.6$  years (range: 18–29 years), and their mean BMI was  $27.2 \pm 6.6$  kg/m<sup>2</sup>. In addition, 20 healthy subjects of matched age and sex were included as a control group. They included 16 female participants (80%) and four male participants (20%) with a mean age of  $20.5 \pm 1.4$  years (range: 18–23 years) and a mean BMI of  $29.3 \pm 6.5$  kg/m<sup>2</sup>.

The mean age of onset was  $15.5 \pm 3.3$  years old, and the mean acne duration was  $5.7 \pm 2.9$  years. Thirty-two patients (53.3%) had post acne hyperpigmentation, while 22 patients (36.6%) only had post acne scars.

Our data revealed that neurotensin serum levels and the scores of the used questionnaires (HADS and PSS-10) of the patient group were significantly higher than those of the control group (Table 1). The mean DLQI score was  $21.43 \pm 5.61$ .

There was a significant positive correlation between serum neurotensin levels and BMI, as well as DLQI scores. Serum neurotensin levels correlated positively with the scores of HADS and PSS-10 as well; however, these correlations were insignificant. A significant positive correlation was found between the scores of the three used questionnaires (Table 2).

Serum levels of neurotensin and the scores of the three questionnaires were significantly elevated in patients with severe acne and in those with post acne scars and hyperpigmentation (Table 3).

## DISCUSSION

In the present study, serum levels of neurotensin were investigated in patients with AV and a group of healthy control subjects. To the best of our knowledge, serum levels of neurotensin have not been previously evaluated in AV. Results of the current work showed that there was a significant increase in serum neurotensin levels in the patient group compared to the control group. There was also a significant relationship between serum levels of neurotensin and DLQI scores.

Acne has a significant impact on QoL, particularly in adolescent and young adult patients.<sup>8</sup> In recent years, there has been a constant preoccupation with the QoL of the patients. QoL represents the degree of well-being that a person feels in different aspects; physical, psychoemotional, social and relational, personal development, and self-determination and rights. Regarding dermatological diseases, taking the impact of the skin disorder in consideration can assist the doctor in finding the best therapeutic proposal and detecting those patients who might be psychologically affected even when the clinical picture of the disease seems mild.<sup>9</sup>

Our study showed that AV affects patient QoL extremely (the mean DLQI score was 21.43). This is in agreement with Al-Shidhani et al,<sup>10</sup> who highlighted that acne has a great impact on patient QoL. Chillicka et al<sup>11</sup> also confirmed the extreme effects of acne on patient QoL, measured using DLQI. Their work also showed

great improvement in the patients' general QoL after applying a series of cosmetological treatments.

The reliability of HADS in detecting anxiety and depression and evaluating their severity in different dermatologic diseases has been previously demonstrated.<sup>12</sup> The present study showed that there was a significant elevation in anxiety and depression scores in patients with acne using HADS. Solgajová et al<sup>13</sup> reported that anxiety and depression are prevalent in 55.6 percent and 37.5 percent of patients with acne, respectively. Uhlenhake et al<sup>14</sup> reported that depression is 2 to 3 times as prevalent in patients with acne than in the general population. Jagtiani et al<sup>15</sup> reported that the frequency of depression was 8.8 percent among patients with AV. AV is among the dermatological diseases with psychological comorbidities. High levels of anxiety, depression, and social anxiety were documented in a sample of dermatology patients, including patients with AV.<sup>16,17</sup> In contrast to these findings, Duman et al<sup>18</sup> concluded that acne does not have any association with depression and anxiety, however, this may be related to the nature of their studied sample. About 73 percent of their sample had mild or moderate AV. In our study, using PSS-10 revealed that patients with acne are suffering from stress. This is in agreement with Yosipovitch et al<sup>19</sup> and Law et al.<sup>20</sup>

Our study showed that there was a significant positive correlation between neurotensin serum levels and BMI. Li et al<sup>21</sup> reported elevated serum levels of proneurotensin in patients with obesity. The stress of living with obesity could possibly explain this positive relationship.<sup>22</sup>

We found significantly positive correlations between the scores of the used questionnaires, indicating a relationship between the degree of QoL impairment and stress, depression, and anxiety in patients with acne. When QoL of patients with acne is impaired, the risk of anxiety and depression increases due to the effect that acne has on body image, which is considered the principal factor related to depression and anxiety.<sup>23,24</sup> This means that the psychological impact of acne results mainly from the patient's perception of the disturbed QoL.

We did not find significant sex differences regarding the serum levels of neurotensin or the scores of any of the used questionnaires.

Previous studies have reported that both sexes are concerned equally about their appearance.<sup>18,23,25</sup> Moreover, in different dermatologic diseases, no significant difference between men and women regarding depression were detected.<sup>24</sup>

Another study reported that the self-esteem of girls with acne was more affected than that of boys.<sup>26</sup> Kellett and Gawkrödger<sup>27</sup> reported that the psychological impact of acne in women was significantly higher than that in men, despite the more severe acne in the male patients. Aktan et al<sup>28</sup> reported that HADS-Depression scores of boys and girls with acne were not significantly different, whereas HADS-Anxiety scores of girls with acne were significantly higher than those of boys with acne. In Al-Shidhani et al's<sup>10</sup> study, the general QoL of the female patients was more affected than that of the male patients. On the other hand, Abdel-Hafez et al<sup>29</sup> reported higher impact of acne in men than in women. They explained this difference by the limited public display of women's faces in Middle Eastern societies.

The present study found a significant elevation in serum neurotensin levels and the scores of the used questionnaires in severe AV. There is some debate about this point. While some authors<sup>30–32</sup> reported a relation between acne severity and the degree of QoL impairment, as well as the psychological affection, others<sup>33–36</sup> did not.

The current findings showed that post acne scars and hyperpigmentation affected

**TABLE 1.** Serum levels of neurotensin and questionnaire scores in the studied groups

GROUP	CASES (N=60)	CONTROLS (N=20)	MANN- WHITNEY TEST	P-VALUE
	MEAN±SD	MEAN±SD		
Neurotensin (pg/mL)	357.59±509.84	51.73±27.05	5.45	<0.001* (HS)
HADS-Depression	13.78±4.4	9.45±1.36	4.32	<0.001** (HS)
HADS-Anxiety	13.83±4.45	9.05±1.09	4.74	<0.001** (HS)
PSS-10	27.9±7.85	18.35±4.65	5.13	<0.001** (HS)

P<0.05 is significant  
 \*Mann-Whitney test  
 \*\*Independent Student's t-test  
 HS: highly significant; HADS: Hospital Anxiety and Depression Scale; PSS-10: Perceived Stress Scale

**TABLE 2.** Correlation between serum levels of neurotensin and questionnaire scores and some clinical criteria

VARIABLE (N=60)	NEUROTENSIN		DLQI		HADS- DEPRESSION		HADS-ANXIETY	
	rho	P-VALUE	r	P-VALUE	r	P-VALUE	r	P-VALUE
Age (years)	-0.01	0.95	-0.14	0.27	0.01	0.95	-0.07	0.62
Age of onset (years)	-0.03	0.84	-0.21	0.11	-0.09	0.49	-0.21	0.10
Duration (years)	0.05	0.67	0.16	0.23	0.18	0.18	0.13	0.30
BMI (kg/m <sup>2</sup> )	0.27	0.036 (S)	0.08	0.56	-0.02	0.89	-0.12	0.37
DLQI	0.27	0.038 (S)	1.00	N/A	N/A	N/A	N/A	N/A
HADS-Depression	0.03	0.82	0.71	<0.001 (HS)	1.00	N/A	N/A	N/A
HADS-Anxiety	0.11	0.41	0.62	<0.001 (HS)	0.56	<0.001 (HS)	1.00	N/A
PSS-10	0.15	0.26	0.68	<0.001 (HS)	0.66	<0.001 (HS)	0.69	<0.001 (HS)

S: significant difference (P<0.05); HS: highly significant difference (P<0.001); rho: Spearman correlation coefficient; r: Pearson correlation coefficient; DLQI: Dermatology Life Quality Index; HADS: Hospital Anxiety and Depression Scale; PSS-10: Perceived Stress Scale; N/A: not applicable

**TABLE 3.** Relationship between neurotensin serum levels and questionnaire scores

VARIABLES		NO.	NEUROTENSIN		DLQI		HADS-DEPRESSION		HADS-ANXIETY		PSS-10	
			MEAN±SD	P-VALUE	MEAN±SD	P-VALUE	MEAN±SD	P-VALUE	MEAN±SD	P-VALUE	MEAN±SD	P-VALUE
Sex <sup>d</sup>	Female	50	381.17±528.18	0.81	21.42±5.71	0.58	13.6±4.23	0.97	13.6±4.34	0.37	27.32±7.81	0.20
	Male	10	237.7±400.9		21.5±5.4		14.7±5.33		15±5.08		30.8±7.8	
Post acne scar <sup>e</sup>	No	38	98.4±38.07	<0.001 (HS)	19.37±5.85	<0.001 (HS)	12.24±4.13	<0.001 (HS)	12.47±4.54	0.001 (S)	25.08±8.11	<0.001 (HS)
	Yes	22	804.37±628.3		25±2.69		16.45±3.55		16.18±3.22		32.77±4.23	
Disease grade <sup>f</sup>	Mild	20	99.82±38.4	0.001 (S)	14.75±3.24	<0.001 (HS)	8.9±0.85	<0.001 (HS)	8.85±0.81	<0.001 (HS)	18.5±3.9	<0.001 (HS)
	Moderate	20	177.52±304.68		24.5±2.98 <sup>a</sup>		15.85±3.15 <sup>a</sup>		15.65±3.18 <sup>a</sup>		31.95±4.32 <sup>a</sup>	
	Severe	20	794.42±636.69 <sup>ab</sup>		25.05±2.78 <sup>a</sup>		16.6±3.41 <sup>a</sup>		17±3.26 <sup>a</sup>		33.25±4.14 <sup>a</sup>	
Pigmentation <sup>g</sup>	No	28	95.44±37.81	0.002 (S)	17.71±5.6	<0.001 (HS)	11.32±4.19	<0.001 (HS)	11.71±4.53	<0.001 (HS)	23.5±8.18	<0.001 (HS)
	Yes	32	586.35±613.04		24.69±3.04		15.94±3.37		15.69±3.5		31.75±5.12	

<sup>a</sup>Significant difference compared to mild cases

<sup>b</sup>Significant difference compared to moderate cases

<sup>d</sup>Student's t-test

<sup>f</sup>Analysis of variance (ANOVA)

S: significant difference (P<0.05); HS: highly significant difference (P<0.001); DLQI: Dermatology Life Quality Index; HADS: Hospital Anxiety and Depression Scale; PSS-10: Perceived Stress Scale

patient QoL and were associated with depression, anxiety, and stress. This is in agreement with Hazarika and Rajaprabha.<sup>37</sup> Brown et al<sup>38</sup> highlighted the high levels of anxiety and the poor QoL in patients with facial post acne scars. The significant impact of post acne scars on the QoL of young adults highlights the necessity of suitable education programs targeting teenagers about AV and its complications, including post acne scarring and hyperpigmentation. These programs may direct the patients with acne to early treatment in order to minimize acne consequences.<sup>39</sup>

## CONCLUSION

It is well known that acne greatly impacts QoL and appears to be associated with depression, anxiety, and stress. Based on our results, serum neurotensin could be a promising marker to objectively evaluate the psychosocial impact of AV.

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